

WHAT IS CLAIMED IS:

1. A method of preparing a pharmaceutical retinoid composition, comprising the step of admixing at least one retinoid or a derivative thereof with dimyristoyl phosphatidylcholine, soybean oil, tertiarybutyl alcohol and water, wherein said admixing produces a mixture comprising liposomes in combination with the at least one retinoid or derivative thereof.
2. The method of claim 1, wherein said retinoid comprises *N*-(4-hydroxyphenyl) retinamide.
3. The method of claim 1, wherein said derivative thereof comprises at least one derivative of *N*-(4-hydroxyphenyl) retinamide.
4. The method of claim 1, wherein said method further comprises the step of admixing at least one additional agent with one or more of said retinoid, dimyristoyl phosphatidylcholine, soybean oil, tertiarybutyl alcohol or water.
5. The method of claim 4, wherein said agent further comprises a linking moiety attached to said agent and one or more lipids attached to said linking moiety.
6. The method of claim 5, wherein said one or more lipids are the same as said at least one lipid.
7. The method of claim 4, wherein said agent comprises a diagnostic agent.
8. The method of claim 4, wherein said agent comprises a targeting agent.
9. The method of claim 8, wherein said targeting agent comprises at least one antibody to a tumor.

10. The method of claim 4, wherein said agent comprises an additional therapeutic agent.

11. The method of claim 10, wherein said additional therapeutic agent comprises an anticancer agent.

12. The method of claim 11, wherein the anticancer agent is chemotherapy agent, a radiotherapy agent, an immune therapy agent, a genetic therapy agent, a hormonal therapy agent, a biological agent, an additional retinoid or a retinoid derivative.

13. The method of claim 1, wherein said dimyristoyl phosphatidylcholine and said soybean oil comprise a ratio of greater than 80:20 during admixing.

14. The method of claim 13, wherein said dimyristoyl phosphatidylcholine and said soybean oil comprise a ratio of greater than 85:15 during admixing.

15. The method of claim 14, wherein said dimyristoyl phosphatidylcholine and said soybean oil comprise a ratio of greater than 90:10 during admixing.

16. The method of claim 15, wherein said dimyristoyl phosphatidylcholine and said soybean oil comprise a ratio of greater than 95:5 during admixing.

17. The method of claim 1, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:5 during admixing.

18. The method of claim 17, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:8 during admixing.

19. The method of claim 18, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:10 during admixing.

20. The method of claim 19, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:12 during admixing.

21. The method of claim 20, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:15 during admixing.

22. The method of claim 21, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:17 during admixing.

23. The method of claim 22, wherein the ratio of retinoid or a derivative thereof to lipid is greater than 1:20 during admixing.

24. The method of claim 1, wherein said water comprises greater than 1% during admixing.

25. The method of claim 24, wherein said water comprises greater than 2% during admixing.

26. The method of claim 25, wherein said water comprises greater than 4% during admixing.

27. The method of claim 26, wherein said water comprises greater than 6% during admixing.

28. The method of claim 27, wherein said water comprises greater than 8% during admixing.

29. The method of claim 28, wherein said water comprises greater than 10% during admixing.

30. The method of claim 1, further comprising freezing said mixture.

31. The method of claim 1, further comprising lyophilizing said mixture.

32. The method of claim 31, wherein said lyophilizing produces a powder.

33. The method of claim 31, further comprising resuspending said mixture with an aqueous solvent.

34. The method of claim 33, wherein said aqueous solvent comprises a pharmaceutically acceptable saline solution.

35. The method of claim 1, wherein greater than 90% of said retinoid or a derivative thereof is incorporated into said liposomes.

36. The method of claim 35, wherein greater than 91% of said retinoid or a derivative thereof is incorporated into said liposomes.

37. The method of claim 36, wherein greater than 92% of said retinoid or a derivative thereof is incorporated into said liposomes.

38. The method of claim 37, wherein greater than 93% of said retinoid or a derivative thereof is incorporated into said liposomes.

39. The method of claim 38, wherein greater than 94% of said retinoid or a derivative thereof is incorporated into said liposomes.

40. The method of claim 39, wherein greater than 95% of said retinoid or a derivative thereof is incorporated into said liposomes.

41. The method of claim 40, wherein greater than 96% of said retinoid or a derivative thereof is incorporated into said liposomes.

42. A method of preparing a pharmaceutical retinoid composition, comprising the step of admixing *N*-(4-hydroxyphenyl) retinamide or a derivative thereof with dimyristoyl phosphatidylcholine, soybean oil, tertiarybutyl alcohol and water, wherein said admixing produces a mixture comprising liposomes in combination with the *N*-(4-hydroxyphenyl) retinamide or a derivative thereof.

43. A pharmaceutical retinoid composition comprising *N*-(4-hydroxyphenyl) retinamide, or a derivative thereof, encapsulated in a lipid material, wherein said lipid material comprises dimyristoyl phosphatidylcholine and soybean oil.

44. The pharmaceutical composition of claim 43, wherein said dimyristoyl phosphatidylcholine and soybean oil comprise a ratio of greater than 80:20.

45. The pharmaceutical composition of claim 43, wherein said composition further comprises at least one additional agent.

46. The pharmaceutical composition of claim 45, wherein said agent further comprises a linking moiety attached to said agent and one or more lipids of said lipid material attached to said linking moiety.

47. The pharmaceutical composition of claim 45, wherein said agent comprises a targeting agent.

48. The pharmaceutical composition of claim 47, wherein said targeting agent comprises at least one antibody to a tumor.

49. The pharmaceutical composition of claim 45, wherein said agent comprises an additional therapeutic agent.

50. The pharmaceutical composition of claim 49, wherein said additional therapeutic agent comprises an anticancer agent.

51. The method of claim 50, wherein the anticancer agent is chemotherapy agent, a radiotherapy agent, an immune therapy agent, a genetic therapy agent, a hormonal therapy agent, a biological agent, an additional retinoid or a retinoid derivative.

52. The pharmaceutical composition of claim 43, wherein said composition is comprised as a lyophilized material.

53. The pharmaceutical composition of claim 43, wherein said composition is comprised in a pharmaceutically acceptable aqueous medium.

54. A method of treating a subject having cancer, comprising administering to said individual a therapeutically effective amount of a composition comprising N-(4-hydroxyphenyl) retamide, or a derivative thereof, encapsulated in a lipid material, wherein said lipid material comprises dimyristoyl phosphatidylcholine and soybean oil.

55. The method of claim 54, wherein said dimyristoyl phosphatidylcholine and soybean oil comprise a ratio of greater than 80:20.

56. The method of claim 54, wherein said composition is comprised in a pharmaceutically acceptable aqueous medium.

57. The method of claim 54, wherein said method further comprises administering at least one additional therapeutic agent to said individual.

58. The method of claim 58, wherein said agent is comprised in said composition.

59. The method of claim 57, wherein said additional therapeutic agent comprises at least one anticancer agent.

60. The method of claim 59, wherein the anticancer agent is chemotherapy agent, a radiotherapy agent, an immune therapy agent, a genetic therapy agent, a hormonal therapy agent, a biological agent, an additional retinoid or a retinoid derivative.

61. A method for increasing growth inhibitory effects of fenretinide on a cell comprising providing to a cell, in combination with fenretinide, one or more agents that increases the level of nitric oxide (NO) in said cell.

62. The method of claim 61, wherein said cell is a tumor cell.

63. The method of claim 62, wherein said tumor cell is a breast cancer cell.

64. The method of claim 63, wherein the breast cancer cell is an estrogen receptor (ER)-positive cell.

65. The method of claim 63, wherein the breast cancer cell is an estrogen receptor (ER)-negative cell.

66. The method of claim 61, wherein fenretinide is provided before the one or more agents.

67. The method of claim 61, wherein fenretinide is provided at the same time as the one or more agents.

68. The method of claim 61, wherein fenretinide is provided after the one or more agents.

69. The method of claim 61, wherein fenretinide is provided more than once.

70. The method of claim 69, wherein fenretinide is provided daily for three months with monthly three-day interruptions.

71. The method of claim 61, wherein said agent is provided more than once.
72. The method of claim 61, wherein said agent is a nucleic acid.
73. The method of claim 72, wherein said nucleic acid is an expression construct encoding iNOS, interferon- γ or herceptin.
- 5 74. The method of claim 61, wherein said agent is a protein.
75. The method of claim 74, wherein said protein is iNOS, interferon- γ or herceptin.
76. The method of claim 61, wherein said agent is a chemopharmaceutical.
77. The method of claim 76, wherein said agent is cyclosporin A.
78. The method of claim 62, wherein said cell tumor cell is a patient.
- 10 79. The method of claim 78, wherein said cell tumor cell is part of a tumor mass in said patient.
80. The method claim 78, wherein providing comprises direct administration to said tumor cell.
81. The method of claim 61, further comprising providing to said cell an additional anti-cancer therapy.
- 15 82. The method of claim 81, wherein said additional anti-cancer therapy is radiation.
83. The method of claim 81, wherein said additional anti-cancer therapy is a distinct chemotherapy.
84. The method of claim 81, wherein said additional anti-cancer therapy is a distinct gene therapy.
- 20 85. The method of claim 81, wherein said additional anti-cancer therapy is immunotherapy.

86. The method of claim 81, wherein said additional anti-cancer therapy is hormonal therapy.
87. The method of claim 61, wherein fenretinide is provided in an amount sufficient to achieve an intracellular concentration of 0.1 μM .
- 5 88. The method of claim 61, wherein fenretinide is provided in an amount sufficient to achieve an intracellular concentration of 0.5 μM .
89. The method of claim 61, wherein fenretinide is provided in an amount sufficient to achieve an intracellular concentration of 1.0 μM .
90. The method of claim 61, wherein said cell is killed.
- 10 91. A method for treating cancer in a subject comprising providing to said subject, in combination, fenretinide and one or more agents that increases the level of nitric oxide (NO) in cancer cells in said subject.
92. The method of claim 91, wherein said cancer is a breast cancer.
93. The method of claim 92, wherein cells of said breast cancer are estrogen receptor (ER)-positive.
- 15 94. The method of claim 92, wherein cells of said breast cancer are estrogen receptor (ER)-negative.
95. The method of claim 91, wherein fenretinide is provided before the one or more agents.
- 20 96. The method of claim 91, wherein fenretinide is provided at the same time as the one or more agents.
97. The method of claim 91, wherein fenretinide is provided after the one or more agents.
98. The method of claim 91, wherein fenretinide is provided more than once.

99. The method of claim 98, wherein fenretinide is provided daily for three months with monthly three-day interruptions.
100. The method of claim 91, wherein said agent is provided more than once.
101. The method of claim 91, wherein said agent is a nucleic acid.
- 5 102. The method of claim 101, wherein said nucleic acid is an expression construct encoding iNOS, interferon- γ or herceptin.
103. The method of claim 91, wherein said agent is a protein.
104. The method of claim 103, wherein said protein is iNOS, interferon- γ or herceptin.
105. The method of claim 91, wherein said agent is a chemopharmaceutical.
- 10 106. The method of claim 105, wherein said agent is cyclosporin A.
107. The method claim 91, wherein providing comprises direct administration to said tumor cell.
108. The method of claim 91, further comprising providing to said cell an additional anti-cancer therapy.
- 15 109. The method of claim 108, wherein said additional anti-cancer therapy is radiation.
110. The method of claim 108, wherein said additional anti-cancer therapy is a distinct chemotherapy.
111. The method of claim 108, wherein said additional anti-cancer therapy is a distinct gene therapy.
- 20 112. The method of claim 108, wherein said additional anti-cancer therapy is immunotherapy.
113. The method of claim 108, wherein said additional anti-cancer therapy is hormonal therapy.

114. The method of claim 91, wherein fenretinide is provided in an amount sufficient to achieve an intracellular concentration in cancer cells of 0.1 μm .
115. The method of claim 91, wherein fenretinide is provided in an amount sufficient to achieve an intracellular concentration in cancer cells of 0.5 μm .
- 5 116. The method of claim 91, wherein fenretinide is provided in an amount sufficient to achieve an intracellular concentration in cancer cells of 1.0 μm .
117. The method of claim 91, wherein fenretinide is provided at 10 mg/day.
118. The method of claim 91, wherein fenretinide is provided at 100 mg/day.
119. The method of claim 91, wherein fenretinide is provided at 200 mg/day.
- 10 120. A composition of matter comprising fenretinide and an agent that increases the level of nitric oxide (NO) in a cell.
121. The composition of claim 120, wherein said agent is a nucleic acid.
122. The composition of claim 121, wherein said nucleic acid is an expression construct encoding iNOS, interferon- γ or herceptin.
- 15 123. The composition of claim 120, wherein said agent is a protein.
124. The composition of claim 123, wherein said protein is iNOS, interferon- γ or herceptin.
125. The composition of claim 129, wherein said agent is a chemopharmaceutical.
126. The composition of claim 125, wherein said agent is cyclosporin A.
- 20 127. The composition of claim 120, wherein said composition is encapsulated in a lipid material.
128. The composition of claim 127, wherein said liposome comprises dimyristoyl phosphatidylcholine and soybean oil.

